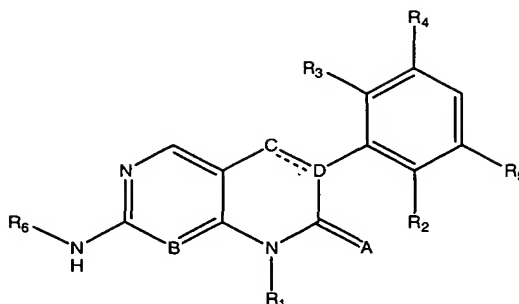


-101-
CLAIMS

What is claimed is:

1. A compound of the formula:



5 wherein:

A is O, NH₂, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)₂, or -NHC(O)-NHR₁₂;

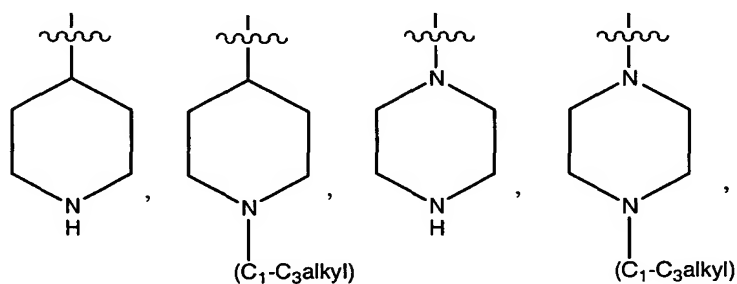
R₁₂ is C₁-C₆ straight or branched chain alkyl, or -(CH₂)_n-C₃-C₈ cycloalkyl ring; n is an integer of from 1 to 3;

10 B, C and D are independently selected from CH or N, with the proviso that C and D are not both N;

R₁ is selected from the group of C₁-C₆ straight or branched chain alkyl, optionally substituted by -COOH, or;

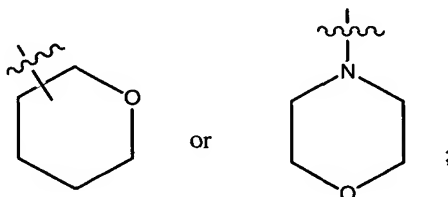
15 a) a phenyl, benzyl or C₃-C₈ cycloalkyl ring, or -CH₂-C₃-C₈ cycloalkyl ring, with the phenyl, benzyl or cycloalkyl rings being optionally substituted by 1 or 2 COOH or -CH₂-COOH groups; or

b) a piperidine or piperazine moiety selected from group of:



the rings of the piperidine or piperazine moieties being optionally substituted by 1 or 2 COOH or -CH₂-COOH groups; or

c) a tetrahydropyran or morpholine moiety of the formulae:



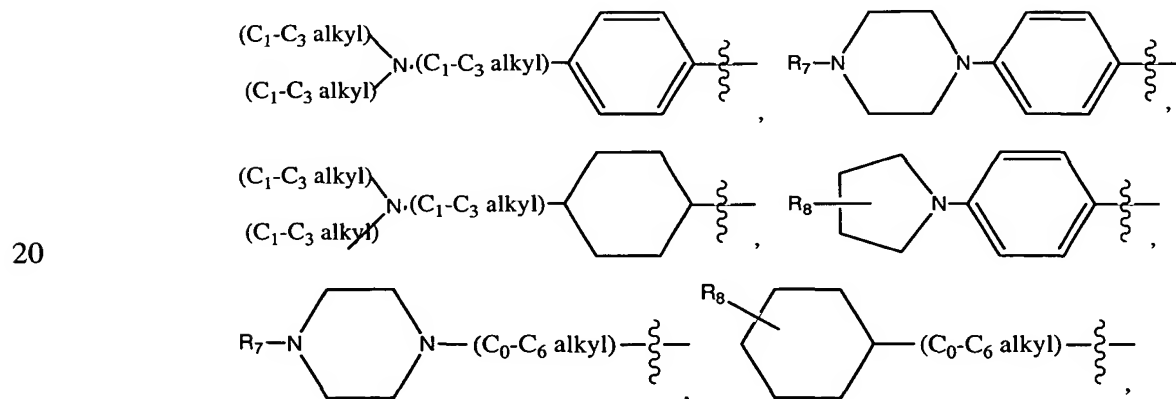
5 R_2 is H, Cl or F;

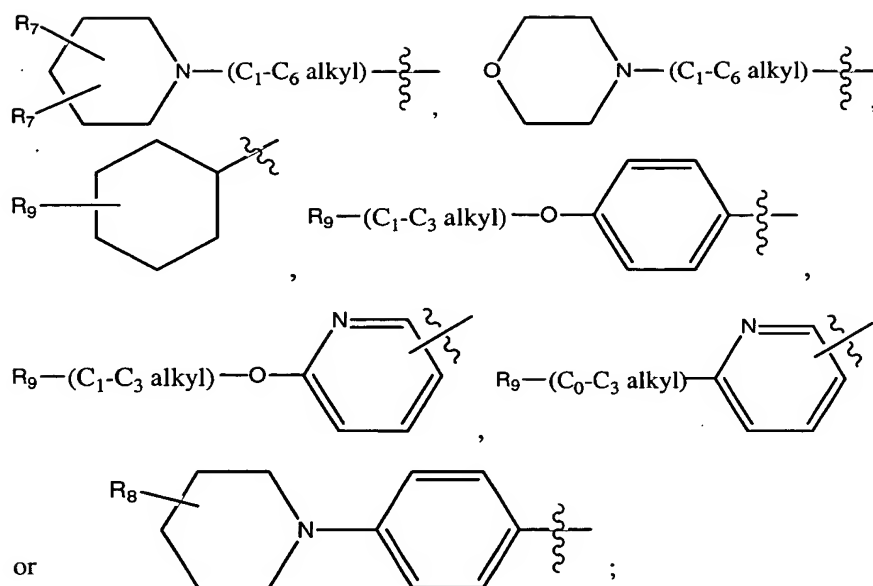
R_3 is H, Cl or F, with the proviso that at least one of R_2 or R_3 is F;

R_4 is H, OH, -OCH₃, or -OCH₂CH₃, with the proviso that, if R_4 is H, R_2 and R_3 are not H;

R_5 is -OCH₃, or -OCH₂CH₃;

10 R_6 is selected from the group of H, -(C₁-C₅ alkyl)-NH₂, -(C₁-C₅ alkyl)-NH-(C₁-C₃ alkyl)-R₁₁, -(C₁-C₅ alkyl)-N-(C₁-C₃ alkyl-R₁₁)₂, -O-(C₁-C₅ alkyl)-NH₂, -O-(C₁-C₅ alkyl)-NH-(C₁-C₃ alkyl)-R₁₁, -O-(C₁-C₅ alkyl)-N-(C₁-C₃ alkyl-R₁₁)₂, -CH(CH₂OH)₂, -(C₁-C₃ alkyl)-(CH₂OH)₂, -(C₁-C₃ alkyl)-O-(C₁-C₃ alkyl)-R₁₁, -(C₁-C₃ alkyl)-O-(C₁-C₃ alkyl)-NH₂, -(C₁-C₃ alkyl)-O-(C₁-C₃ alkyl)-NH-(C₁-C₃ alkyl)-R₁₁, -(C₁-C₃ alkyl)-O-(C₁-C₃ alkyl)-N(C₁-C₃ alkyl-R₁₁)₂, phenyl substituted by one or two groups selected from NH₂, -N(C₁-C₃ alkyl), -N(C₁-C₃ alkyl)₂, CN or -(C₁-C₃ alkyl)-tetrazole, or C₁-C₆ alkyl,





5 with each of the alkyl chains of any group in this R₄ definition being optionally substituted by from 1 to 4 OH groups;

R₇ in each instance is independently selected from H, -NH₂, NH(C₁-C₃ alkyl), N(C₁-C₃ alkyl)₂, or C₁-C₃ alkyl;

R₈ is H, OH or C₁-C₃ alkyl;

10 9 H, OH, -NH₂, NH(C₁-C₃ alkyl), or N(C₁-C₃ alkyl)₂;

R₁₀ is H or C₁-C₃ alkyl;

R₁₁ is H, CN, OH, NH₂, F, or CF₃;

or a pharmaceutically acceptable salt or ester form thereof.

2. A compound of Claim 1 selected from the group of:

15 1-Cyclopentyl-7-(4-diethylamino-butylamino)-3-(2,6-difluoro-3-hydroxy-5-methoxy phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

1-Cyclopentyl-7-(4-diethylamino-butylamino)-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

20 (S,S)-1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-[(5-hydroxymethyl-2-phenyl-[1,3]dioxolan-4-ylmethyl)-amino]-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

(S,S)-1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-(2,3,4-trihydroxy-butylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; or

5 1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-(4-hydroxy-cyclohexylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-(2-hydroxy-1-hydroxymethyl-ethylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

10 7-(3-Amino-2-hydroxy-propylamino)-1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

15 1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-[2-(2-hydroxy-ethoxy)-ethylamino]-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

1-Cyclopropyl-7-(4-diethylamino-butylamino)-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; or

20 7-(4-Diethylamino-butylamino)-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;
or a pharmaceutically acceptable salt or ester form thereof.

3. A compound of Claim 1 selected from the group of:

3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-1-ethyl-7-(2-hydroxy-1-hydroxymethyl-ethylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

25 3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-1-ethyl-7-(4-hydroxy-cyclohexylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-(2,3-dihydroxy-butylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one

30 1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-(2,3-dihydroxy-propylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;
or

7-(4-Amino-2,3-dihydroxy-butylamino)-1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

5 1-Cyclopentyl-3-(2-fluoro-3,5-dimethoxy-phenyl)-7-([S,S]-2,3,4-trihydroxy-butylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-1-ethyl-7-[2-(2-hydroxyethoxy)-ethylamino]-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

10 7-(4-Amino-2,3-dihydroxy-butylamino)-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

7-{3-[Bis-(2-hydroxy-ethyl)-amino]-propylamino}-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; or

15 1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-(2,3-dihydroxy-propylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; or a pharmaceutically acceptable salt or ester form thereof.

4. A compound of Claim 1 selected from the group of:

20 3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-7-(2,3-dihydroxy-butylamino)-1-ethyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

Ethyl-4-[3-(2,6-difluoro-3,5-dimethoxy-phenyl)-7-methylamino-2-oxo-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]-cyclohexanecarboxylate;

25 4-[3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-7-methylamino-2-oxo-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]-cyclohexanecarboxylic acid;

7-Amino-3-(2,6-difluoro-3,5-dimethoxy-phenyl)-1-piperidin-4-yl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; compound with trifluoroacetic acid; or

30 1-Cyclopentyl-3-(2-fluoro-3,5-dimethoxy-phenyl)-7-(2-hydroxy-1-hydroxymethyl-ethylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

1-Ethyl-3-(2-fluoro-3,5-dimethoxy-phenyl)-7-(4-hydroxy-butylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

(S)-1-Cyclopentyl-7-(2,3-dihydroxy-propylamino)-3-(2-fluoro-3,5-dimethoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

5 1-Ethyl-3-(2-fluoro-3,5-dimethoxy-phenyl)-7-(4-hydroxy-cyclohexylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

4-[3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-7-methylamino-2-oxo-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]-piperidine-1-carboxylic acid; or

10 3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-7-methylamino-1-piperidin-4-yl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

3-(2,6-Difluoro-3,5-dimethoxy-phenyl)-7-(2,3-dihydroxy-propylamino)-1-ethyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

15 1-Cyclopentyl-7-(4-diethylamino-butylamino)-3-(3-ethoxy-2,6-difluoro-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

(R)-1-Cyclopentyl-7-(2,3-dihydroxy-propylamino)-3-(2-fluoro-3,5-dimethoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

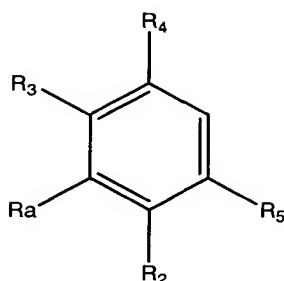
1-Ethyl-3-(2-fluoro-3,5-dimethoxy-phenyl)-7-[2-(2-hydroxy-ethoxy)-ethylamino]-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one; or

20 1-Cyclopentyl-3-(2-fluoro-3,5-dimethoxy-phenyl)-7-(*trans*-4-hydroxy-cyclohexylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one;

or a pharmaceutically acceptable salt or ester form thereof.

5. A pharmaceutical composition comprising a pharmaceutically effective
25 amount of a compound of Claim 1 and a pharmaceutically acceptable carrier.

6. A compound of the formula:



wherein:

R₂ is Cl or F;

R₃ is Cl or F, with the proviso that at least one of R₂ or R₃ is F;

5

R₄ is H, OH, -OCH₃, or -OCH₂CH₃;

R₅ is -OCH₃, or -OCH₂CH₃;

R_a is selected from the group of NH₂, I, CN, -CH₂CN, -C(O)CN, -CH₂OH, -C(O)H, -C(O)OR, -CH₂C(O)OR, -C(O)C(O)OR; and

R is selected from H or C₁-C₆ alkyl.

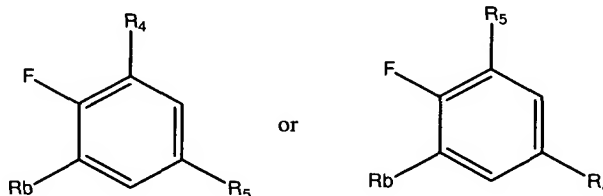
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7. A compound of Claim 9 wherein of R₂ and R₃ are fluorine, and R₄, R₅, R_a, and R are as defined in Claim 10.

8. A compound of Claim 9 wherein of R₂ and R₃ are fluorine, R₄ is -OCH₃, R₅ is -OCH₃ or -OCH₂CH₃, R_a is NH₂, I, CN, -CH₂CN, -C(O)CN, -CH₂OH, -C(O)H, -C(O)OR, -CH₂C(O)OR, or -C(O)C(O)OR; and R is H or C₁-C₆ alkyl.

15

9. A compounds of the formulae:



wherein:

R₄ is H, OH, -OCH₃, or -OCH₂CH₃;

20

R₅ is -OCH₃, or -OCH₂CH₃;

R_b is selected from the group of NH₂, I, CN, -CH₂CN, -C(O)CN, -CH₂OH, -C(O)H, -C(O)OR, -CH₂C(O)OR, and -C(O)C(O)OR; with the proviso that when R_b is -C(O)H, R₄ and R₅ are not both -OCH₃; and

R is selected from H or C₁-C₆ alkyl.